Final Report for AOARD Grant FA2386-10-1-4059

"Study of opto-electronic properties of a single microtubule in the microwave regime"

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Name of Principal Investigators: Anirban Bandyopadhyay
- e-mail address : anirban.bandyo@gmail.com
- Institution : National Institute for Materials science
- Mailing Address : 1-2-1 Sengen, Main Building 815, Tsukuba
- Phone : +81-29-859-2167

Fax : +81-29-859-2801
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Abstract: In biology textbooks, we are taught to believe that biology is all about chemical reactions. However, recent discovery of electromagnetic sensing and antenna like communication of key biomaterials demand for the existence of a world of physical communication and energy exchange squarely parallel to the chemical only biology believed to date. This finding suggests that so-called safe mobile communications (100 kHz to 300 GHz) across the globe are not safe anymore.

The discovery noted above also unravels that from basic protein molecules to the giant biological structure; every part of an integrated biological system absorbs and radiates to communicate in a distinct frequency band. This means, multiple frequency bands operate simultaneously in a biological system and if energy is injected at a local part of any band is distributed all over the entire system. Thus, the biological operational mechanisms and its evolutions are not discrete events as we are taught. Even a linguistic conversation using sound can affect a molecular scale phenomenon and rhythms are eventual expressions that emerge from those molecules. Thus, biological systems like our brain, organs change in every living life form at every moment, define and redefine rhythms of our life (e.g. circadian, cardiac) according to our environment.

Our objective is to develop the algorithm that correlates the environment, biological rhythms and the molecular dynamics at the atomic scale, the triangular connecting route will create a new biology, observed but never seen before.

Introduction: Background: a. Microtubule resonance: International health hazard data suggests that there is no problem with the kHz to

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14. ABSTRACT

In biology textbooks, we are taught to believe that biology is all about chemical reactions. However, recent discovery of electromagnetic sensing and antenna like communication of key biomaterials demand for the existence of a world of physical communication and energy exchange squarely parallel to the chemical only biology believed to date. This finding suggests that so-called safe mobile communications (100 kHz to 300 GHz) across the globe are not safe anymore. The discovery noted above also unravels that from basic protein molecules to the giant biological structure; every part of an integrated biological system absorbs and radiates to communicate in a distinct frequency band. This means, multiple frequency bands operate simultaneously in a biological system and if energy is injected at a local part of any band is distributed all over the entire system. Thus, the biological operational mechanisms and its evolutions are not discrete events as we are taught. Even a linguistic conversation using sound can affect a molecular scale phenomenon and rhythms are eventual expressions that emerge from those molecules. Thus, biological systems like our brain, organs change in every living life form at every moment, define and redefine rhythms of our life (e.g. circadian, cardiac) according to our environment. Our objective is to develop the algorithm that correlates the environment, biological rhythms and the molecular dynamics at the atomic scale, the triangular connecting route will create a new biology, observed but never seen before.

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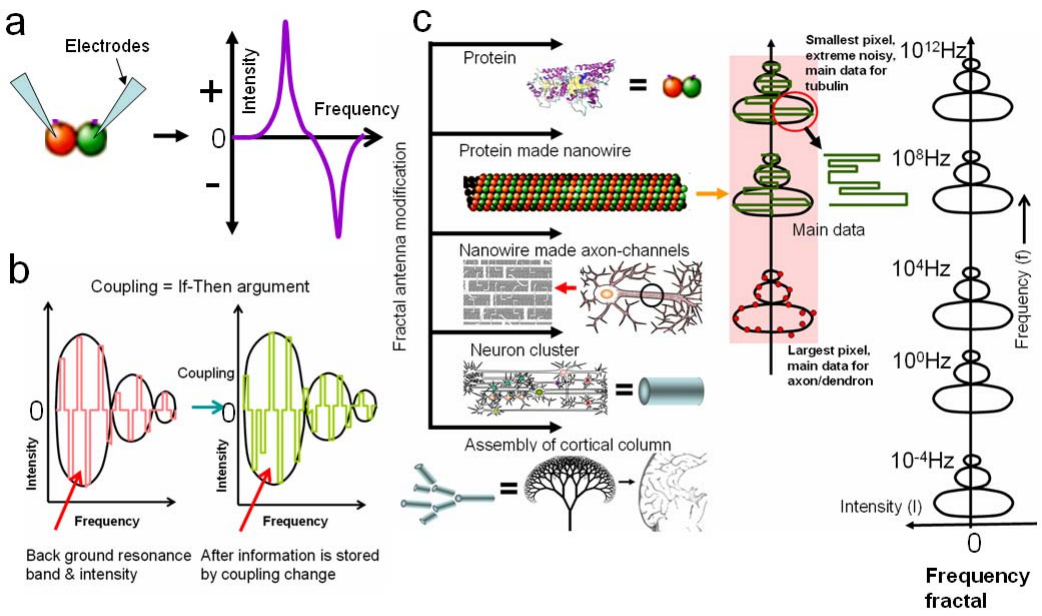
GHz emissions (1). However, Bandyopadhyay group has recently found that proteins and microtubules communicate in the same frequency range, it means, that all mobile phones and wireless communication devices are affecting every single life form in the planet at every moment. Microtubules are hollow cylinders composed of tubulin heterodimer proteins found in all eukaryotes and thus far with 40,000 papers it was strongly believed that it only plays the role of skeleton of a cell and vesicle transport superhighway for a living cell. All those who believed that it might play a role in the information processing were strongly criticized (2).

The faith that biological systems operate only by chemicals has sustained for the last 40 years and toppled just recently. Since Bandyopadhyay group discovered that the biological materials start to oscillate with a natural vibrational frequency when it is triggered with a particular signal (3-4). During this vibration, they communicate (unpublished data, Bandyopadhyay group). There are plenty of sources, e.g. membrane potential, GTP hydrolysis etc pointed out already as sources to feed energy to the resonant oscillations, unused GHz and MHz electromagnetic radiations were detected outside the living cells (5-8). After the discovery of Bandyopadhyay group's bio-resonance, the effect of MHz oscillations is being verified by medical doctors (9). New models are being proposed how actually such resonance could generate in-vivo in the brain to create global and local synchrony of neuron firing via microtubule (10). To put an end to theoretical speculation, Bandyopadhyay group has discovered that even a dc bias could generate oscillations in the microtubules in vivo inside the living neuron cells. Therefore, an alternate form of physical biology squarely parallel to the chemical only biology is taking shape across the globe, e.g. wireless communication model of the brain via microtubule (11) and development of a new biology (12).

b. Mysteries of neuroscience: Molecular neuroscience considers that exchange and interaction of molecules defines the properties observed in biology. Up to now, neural communication is believed to be primarily via Hudgkin-Huxley spiking and secondarily via electronic conduction via gap junctions, and modulated by neurochemicals. In the last 15 years, there have been significant challenges in the literatures starting from Lichtman (13). The list of unexplained mysteries is long; (i) hundreds of dendritic channels carry out logical computations, (ii) the programmability, Neurotransmitters alone cannot Microtubules provide a new dimension for neuronal communication electrically or via mechanical ultrasound vibration. György Buzsáki argued using the physics of oscillations that its a unified journey from neuronal assembly organization to complex cognitive

processing and memory storage (14). Microtubule research takes us to a point when one can experimentally underpin this unified link.

c. Frequency fractal: In fractal, a geometric shape is repeated if a part of it is zoomed, continuously. Fractal is related with the spatial symmetry in nature. Researchers fitted the heartbeat and other rhythms (time-intensity plot) with fractal expressions to find self-similarity. Frequency fractal is very different from that. Bandypadhyay et al replaced x and y spatial co-ordinates of a fractal space with frequency (x,y~f1,f2). Their microtubule research showed that the resonance frequency (see basics of resonance frequency in figure a) plot that represents the stored/processed information exhibits a three unique patterns like the one shown in the figure b in three frequency ranges. The central pattern is the information content in absolute term, not a fitting. The pattern for



a. Tubulin protein resonance measurement, intensity of electromagnetic resonance, positive and negative direction, as a function of frequency. b. Main resonance frequency band for a particular oscillator, say, tubulin or microtubule. Background band is the natural band, after conformational/structural change, the band reformats and this information is stored. c. The construction of frequency fractal, complete bands of microtubule is shown.

Tubulin in the GigaHartz and in the TeraHartz frequency range is found similar to the pattern for microtubules in the megahartz and in the kilohartz range, with a common region (see complete microtubule band in Figure c). The same pattern is found in the microtubule bundles like axon of a neuron in the 500-1kHz range. Recently they found the same pattern for the neuron clusters in the 100Hz range (Mu band of brain). Therefore, this common pattern is named as a "frequency fractal" and it maps an absolute information content pathway (see figure c, right). It is perceived that this fractal cannot die

out in the neuron cluster, even for the larger clusters the same basic pattern should exist. Then, if plotted similarly, all spontaneously generated patterns in a living system would exhibit an identical shape with a little difference (instead of space zoom frequency). A journey through the entire frequency range from 1 milli Hz to 100 Tera Hz defines information content of the entire hardware e.g a single frequency fractal represents the entire brain. At all level, two parameters control the resonance property (i) length of the oscillator, (ii) orientation, and always information is stored/erased by modifying the coupling parameter physically. None of the components looks like a fractal but its information content is. Therefore, an information fractal couples entire brain as a single unit, energy transfer occurs via common overlap band shown in Figure c, we do not need additional wiring two communicate between two distant region of the brain. For the lowest frequency range, the corresponding hardware is the entire brain.

Project achievement: a. Underpin a generic "frequency fractal" pathway: The first phase of the project would be analyzing the data produced so far on rhythm by Poon et al, by implementing the Frequency fractal model of Bandyopadhyay et al. In this phase, we correlate frequency fractal with existing biological rhythms to estimate superposition of multiple rhythms in an apparent spectrum, which was never considered. In this project, we avoid "fitting" and "interpreting", and talk in terms of absolute information content in a peak. At this stage, they will underpin the most critical rhythms to be investigated thoroughly, cardiac, circadian like generic biological rhythms, based on the analysis of the first phase (15).

Project achievement:: b. Create environment interaction map of bio-rhythm by direct animal study: Once a complex bio-rhythm map is filtered as sum of multiple maps, one to one correlation between "frequency fractal" model and bio-rhythms are established. Then we need to estimate how an environment affects the biorhythms and that is translated to the molecular scale and vice versa. Therefore, a series of experiments will be made and bio-hazard estimation simulator will be made. Note that slow wave is important for various reasons (16).

Project achievement:: c. Development of a "Frequency fractal" simulator: Once the simulator is built, the deviation from ideal pattern at every frequency range is the absolute information content, thus, we engage in design and development of a in-situ drug effect, environmental effect analysis machine. Rhythm monitor can support live reporting.

Project achievement:: d. Development of a "frequency fractal" artificial device: Bandyopadhyay group has been developing organic

materials in NIMS that does not necessarily look like fractal, but generates a frequency fractal. This project would continue in MIT, and additional knowledge gathered during the real bio-system data analysis in MIT will be included in developing the device design for a complex analytic hardware development.
These four plans will run in parallel following a cyclic feedback loop.

Novelty of the project: 1. Hidden controls un-earth: Frequency fractal maps an entire hardware as a single mathematical expression. Thus, physical response of any hardware is expressed in all frequency bands in parallel. For example, currently, by heartbeat we mean exactly what we see in the ECG report. However, by frequency fractal concept several unique versions of it are embedded in the higher and in the lower frequency domains, which play an equally important role in governing the beat. All these hidden layers will become known.
Novelty of the project: 2. Predicting for the first time, what is meant by a set of vibration: Any synchronous set of bursts or rhythms in the hardware would not require fitting with a random model. Since we can transform any set of pulses or vibrations in terms of a frequency map and interpret it using simulator, we can capture rhythms of the brain or other organ and interpret it's meaning in absolute terms.
Novelty of the project: 3. Co-existence of physical and chemical biology: For example, neuron firing will not remain a single burst of neurotransmitters as Hudgkin Huxley predicted. Resonant energy transfer and synchronous wireless communication would be incorporated into this model, and the mysterious logical behaviors will be explained. In this way, biological events would undergo certain conceptual modifications.
Novelty of the project: 4. Frequency Fractal electronics and photonics hardwares: There will be a series of products on the frequency fractal hardware. Since (i) Single fractal expression would control a giant machine, (ii) noise free ultra-low power management could be implemented (our Japanese patent JP-2013-19552). The concept is being implemented in a massive artificial brain like computer (AjoChhand project, NIMS, Japan).

Outlook of the project: The project would develop a platform by generating a simulator and complete "frequency fractal" map of at least one organ system of a biological systems. These two products will be the beginning; it will be expanded in the future into multiple systems and into a series of hardware products. It will be attempted during joint project execution for the one year to bring more number of scientists and students interested in using this particular kind of tools that enables looking at the biological system from physical communication perspective. Establishing the chemical+physical

duality of a biological system is an important aspect of the work, for an example, an ac trigger to a neuron below threshold caused chemical firing. Therefore the work does not challenge the existing neuroscience, rather unfolds a world never seen before (http://www.web-books.com/eLibrary/ON/B0/B98/06M98.html).

[1] http://www.icnirp.de/documents/RFReview.pdf
[2] http://arxiv.org/pdf/q-bio/0404007v2.pdf
[3] S. Sahu, et al Applied Physics Letters 102, 123701 (2013)
[4] S. Sahu, et al Biosensors and Bioelectronics 47(2013)141–148 2
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[9] S. Hameroff et al Transcranial Ultrasound (TUS) Effects on Mental States: A Pilot Study. Brain Stimulation, 2013; 6 (3): 409 DOI: 10.1016/j.brs.2012.05.002
[10] S. Hameroff et al Transcranial Ultrasound (TUS) Effects on Mental States: A Pilot Study. Brain Stimulation, 2013; 6 (3): 409 DOI: 10.1016/j.brs.2012.05.002
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[14] http://www.amazon.com/Rhythms-Brain-Gyorgy-Buzsaki/dp/0199828237
[15] http://www.youtube.com/watch?v=Sximg5thMlQ
[16] http://www.sws-book.com/SWS_Book_online_vers.pdf

List of Publications and Significant Collaborations that resulted from your AOARD supported project:

Sahu S, Ghosh S, Ghosh B, Aswani K, Hirata K, Fujita D, et al (2013) Atomic water channel controlling remarkable properties of a single

brain microtubule: correlating single protein to its supramolecular assembly. Biosens Bioelectron 47:141–8;

Sahu S, Ghosh S, Hirata K, Fujita D, Bandyopadhyay A (2013) Multi-level memory-switching properties of a single brain microtubule. Appl Phys Lett 102:123701

Computational myths and mysteries that have grown around microtubule in the last half a century and their possible verification S. Sahu, S. Ghosh, D. Fujita,A. Bandyopadhyay Journal of Computational and Theoretical Nanoscience (Special Issue) 8, 1-7 (2011), (cover page article).

Information 2014, 5(1), 28-100; doi:10.3390/info5010028 Design and Construction of a Brain-Like Computer: A New Class of Frequency-Fractal Computing Using Wireless Communication in a Supramolecular Organic, Inorganic System
Subrata Ghosh, Krishna Aswani, Surabhi Singh, Satyajit Sahu, Daisuke Fujita and Anirban Bandyopadhyay

Patents: Here are the list of the patents. The patent number 2, 9 and 10 are from these projects 2010-2013

A list of the patents filed & issued on our brain building project:

1. A vertical parallel processor (2006) JP-5187804 Anirban Bandyopadhyay, K. Miki (issued 2013)
2. An inductor made of arrayed capacitors (2010) JP-096217 (world patent filed), Satyajit Sahu, Daisuke Fujita, Anirban Bandyopadhyay
3. Thermal noise driven molecular rotor (2013). 13-MS-095; Subrata Ghosh, Satyajit Sahu, Daisuke Fujita, Anirban Bandyopadhyay
4. Sensor, molecular machine, and controller attached programmable nano-robot (2013). 13-MS-097; Subrata Ghosh, Daisuke Fujita, Anirban Bandyopadhyay
5. A molecular chip that generates electrical power from free thermal noise (2013). 13-MS-096; Subrata Ghosh, Daisuke Fujita, Anirban Bandyopadhyay
6. A supramolecular architecture creation by successive phase transitions and radiations (2013). 13-MS-099'; Subrata Ghosh, Daisuke Fujita; Satyajit Sahu, Anirban Bandyopadhyay
7. A supramolecular architecture that forms automatically as the system self-assembles the "if-then" statements of computer programming (2013). 13-MS-100; Anirban Bandyopadhyay, Subrata Ghosh, Daisuke Fujita
8. A computer architecture that uses frequency fractal modulation as

the basis of information processing (2013). 13-MS-101; Subrata Ghosh, Daisuke Fujita, Anirban Bandyopadhyay
9. A chemical synthesis technology in which materials self-assemble such that a particular fractal made of frequency is generated (2013). 13-MS-098; Subrata Ghosh, Daisuke Fujita, Anirban Bandyopadhyay
10. Synthesis of a spiral organic structure wherein the magnetic field produced is the function of the charge stored (2013). 13-MS-102; Satyajit Sahu, Subrata Ghosh, Daisuke Fujita, Anirban Bandyopadhyay

17 conference presentations exclusively on microtubule.

1. Practical realization of nano brain: computing on organic monolayer, 25-27 May Unconventional Computing-2010, Tokyo, Japan
2. Remarkable electronic properties of a single Microtubule Google Mountain view campus, workshop on quantum biology 22 October 2010
3. Paul Davies Beyond Center at Arizona State University (Phoenix) Phoenix, workshop on quantum biology and cancer research, Experimental studies on single microtubule, 25-27 October 2010, Tempe, Arizona State University, USA
4. Quantum aspects of microtubule: Direct experimental evidence for the existence of quantum states in microtubule, Towards a science of consciousness May 2-8 (2011), Sweden
5. Electromagnetic energy of cells and microtubule: how microtubule research will revolutionize the human technologies, EDALC-2011, Czech Republic 1-3 July 2011
6. International Lecture for PhD students: Can we ever make a computer that thinks, creates like human brain? Keio University 24 October (2011)
7. UGC Referesher course lecture series for University & College lecturers; 25th-26th November 2011 North Bengal University, Siliguri, India
Lecture 1: Brain-like computing: synchrony and non-linear frequency pulling to revolutionize human technologies
Lecture 2: Topological insulators, semiconductors, metals: the physics of new generation materials
Lecture 3: Revolutionary technologies of microtubule, hidden in nature for 350 crore years.
8. Vision Talk QUANSAS 2011; Towards inventing the last machine of mankind: the ultimate intelligent machine, nano-brain, Agra 1-4th Dec 2011, India
9. Bio-inspired system Science: IIT Rajasthan 1-3 March 2012
Lecture 1:A new kind of computing far beyond quantum or classical computer: brain inspired computing?
Lecture 2:Remarkable technologies embedded in microtubule:

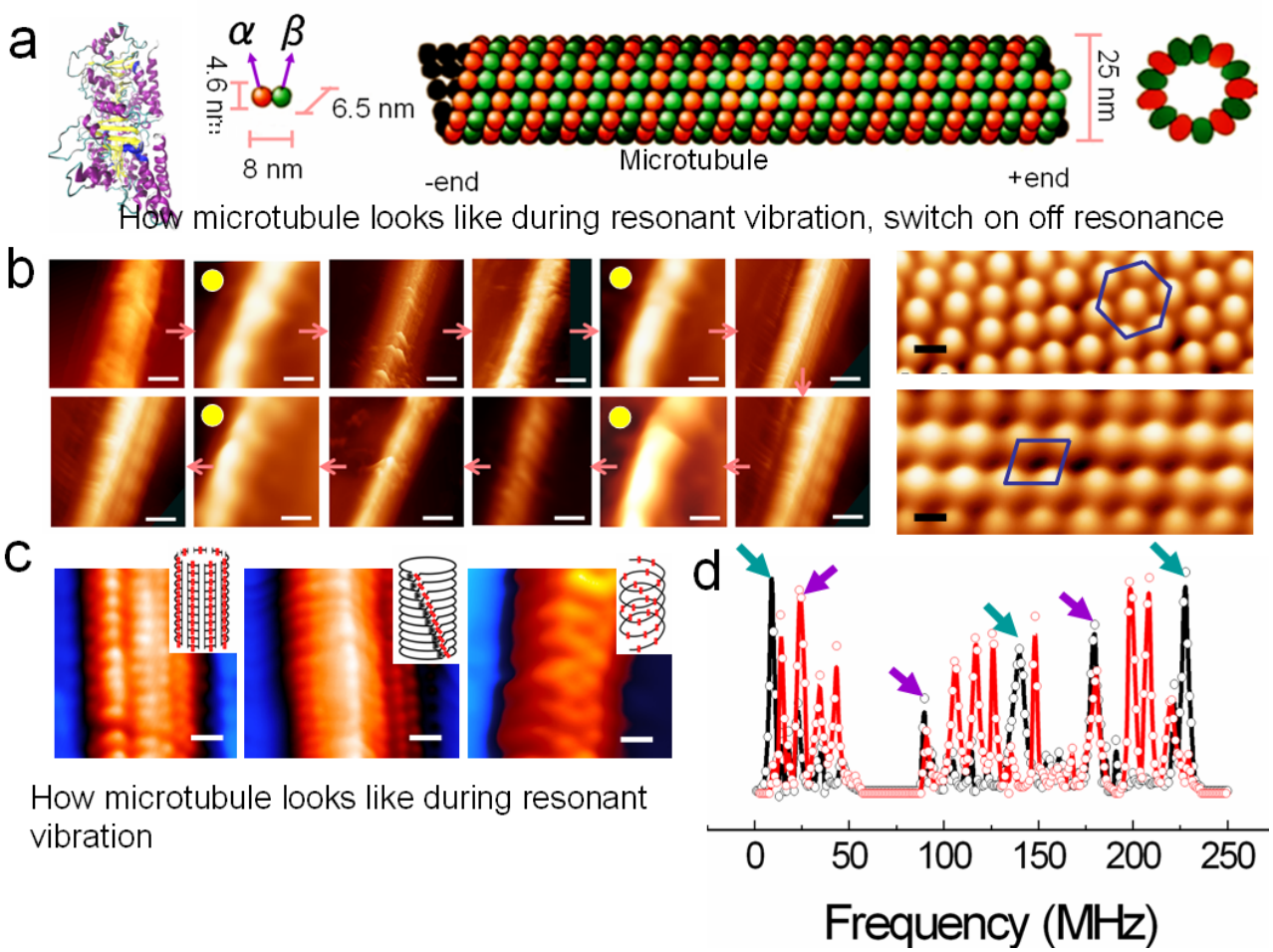
Industrial & Biological perspective
10. Brain mind and the universe: Switzerland 29 March to 3rd April 2012Remarkable electronic properties of microtubule: a detailed rigorous perspective on its information processing
11. Poesis: Brain Science: 25-27 May 2012, Italy, Do we need to go beyond quantum mechanics to explain the brain?
12. IICB international conference 11-13 Sept 2012, India CESIN, Information and communication of a living cell from a complexity engineers perspective
13. JK Lakshmipat, Jaipur, SocPros 2012, 28-30 December, India
Lecture 1: Challenges of the 21st century computing: Will all problems merge to a single problem of computer science?
Lecture 2: The remarkable engineering of microtubule: A perspective
14. TSC 2013, Agra, India 2-9 March Ten remarkable technologies of microtubule.
15. University of Tokyo, Wireless computing with an antenna and a space-time tensor: a new world of computing, May 16, 2013
16. Indian Institute of Technology, Roorki, India Can we build a brain like computer? August 16, 2013
17. QUANSAS 2013 Measurement of a single neuron cell and discovery of a frequency fractal 28 November 2013

Attachments: Publications a), b) and c) listed above if possible.

DD882: As a separate document, please complete and sign the inventions disclosure form.

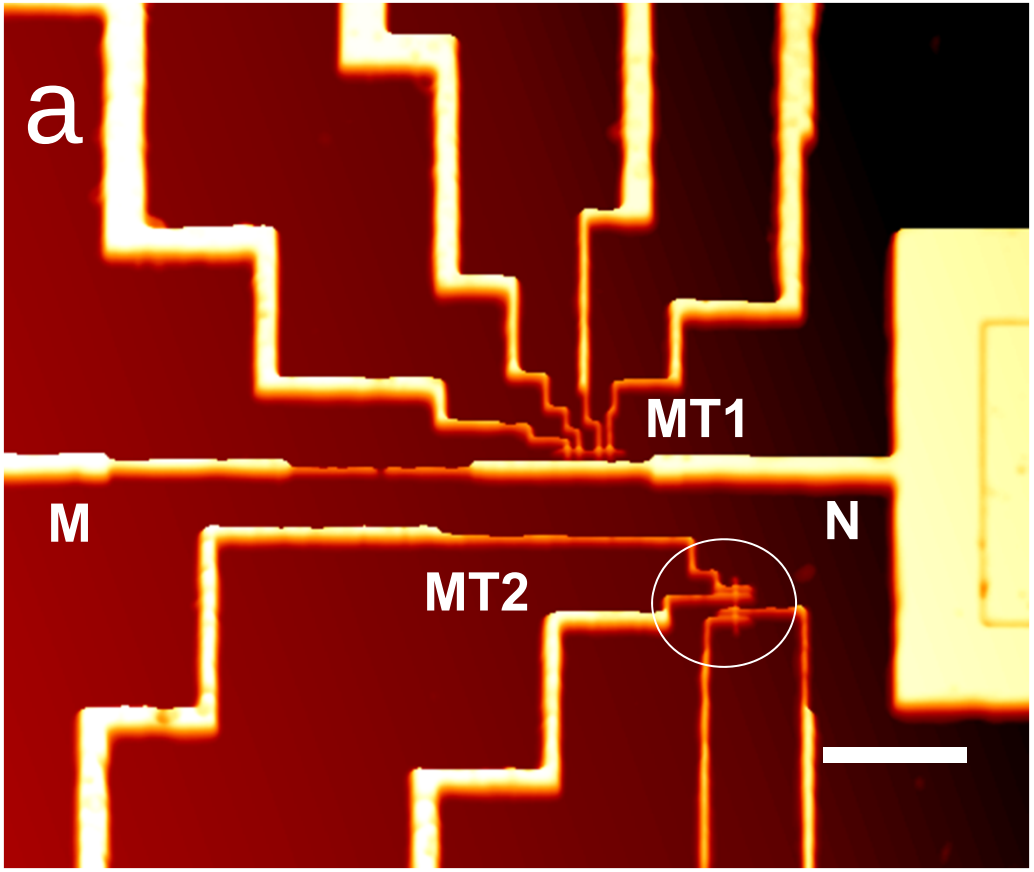
Important Note: If the work has been adequately described in refereed publications, submit an abstract as described above and refer the reader to your above List of Publications for details. If a full report needs to be written, then submission of a final report that is very similar to a full length journal article will be sufficient in most cases. This document may be as long or as short as needed to give a fair account of the work performed during the period of performance. There will be variations depending on the scope of the work. As such, there is no length or formatting constraints for the final report. Keep in mind the amount of funding you received relative to the amount of effort you put into the report. For example, do not submit a $300k report for $50k worth of funding; likewise, do not submit a $50k report for $300k worth of funding. Include as many charts and figures as required to explain the work.

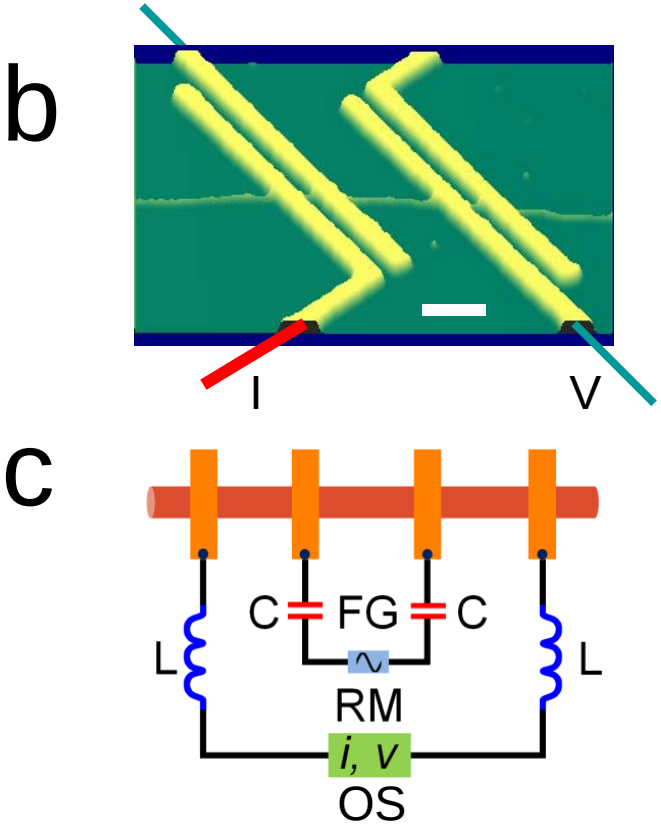
Figure 1



a. Molecular structure of tubulin protein (left). Schematic presentation of a microtubule nanowire. b. Tunneling current image of a single microtubule. Yellow dots represent images, wherein the microtubule is excited with the resonant ac frequency signal between its two ends. The arrow depicts sequence of events. The ac frequencies corresponding to the yellow dots are: first, 9 MHz, second 22MHz, third 113MHz, fourth 228MHz. The scale bar for the images is 10 nm. In the right, two cryo-TEM images, top one shows hexagonal close packing of tubulin proteins and in the bottom we have rectangular close packing. Scale bar 8 nm. The lattice switching is found to occur naturally, reversibly in microtubule. c. Three classes of 2D lattice geometries of tubulin during resonant transmissions. d. Comparison of absorbed (black) and transmitted energy (red) as a function of frequency by a single microtubule. Green arrows depict the peaks that appear in absorption and disappear in transmission. Purple arrows show peaks whose intensity is modified. Rest peaks are newly generated.

Figure 2

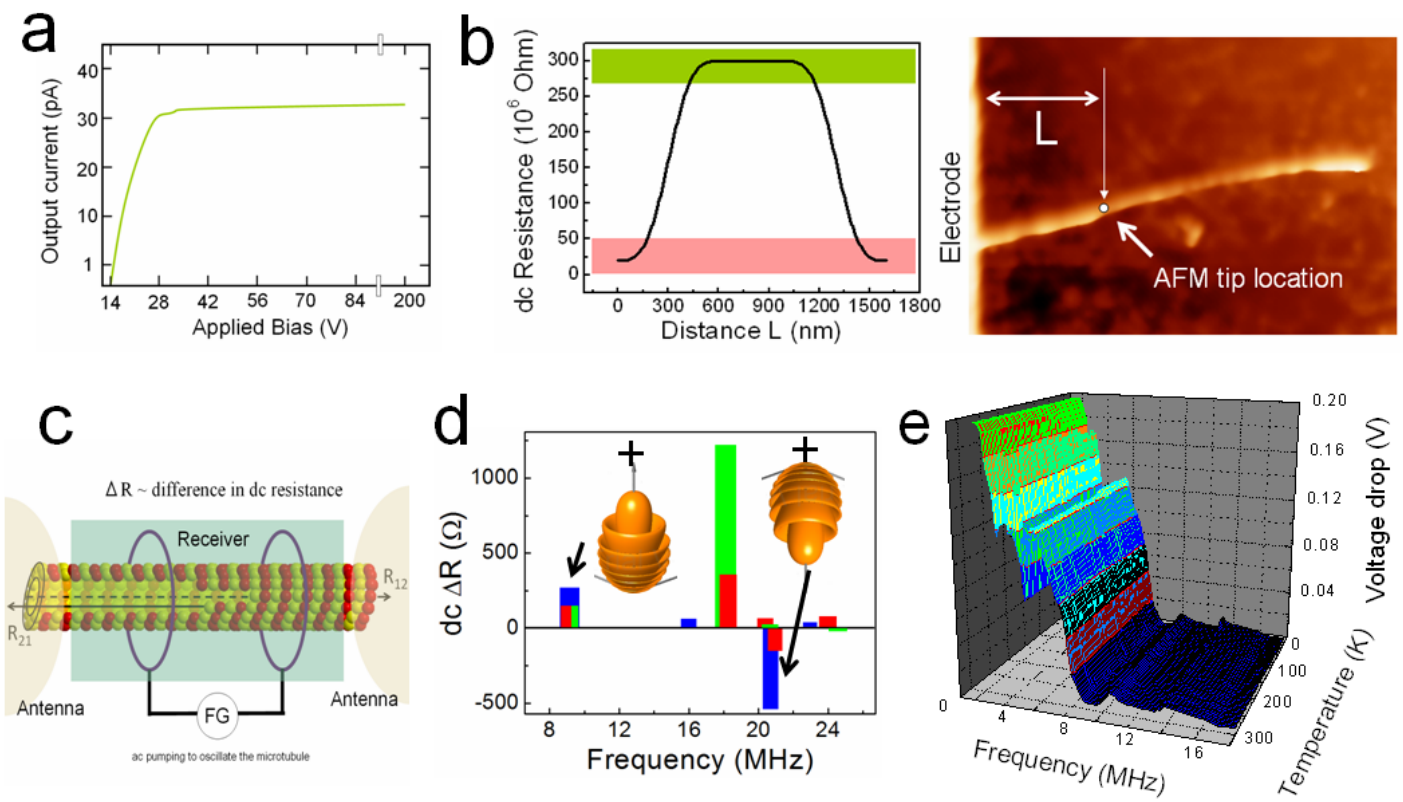




Wireless communication measurement device

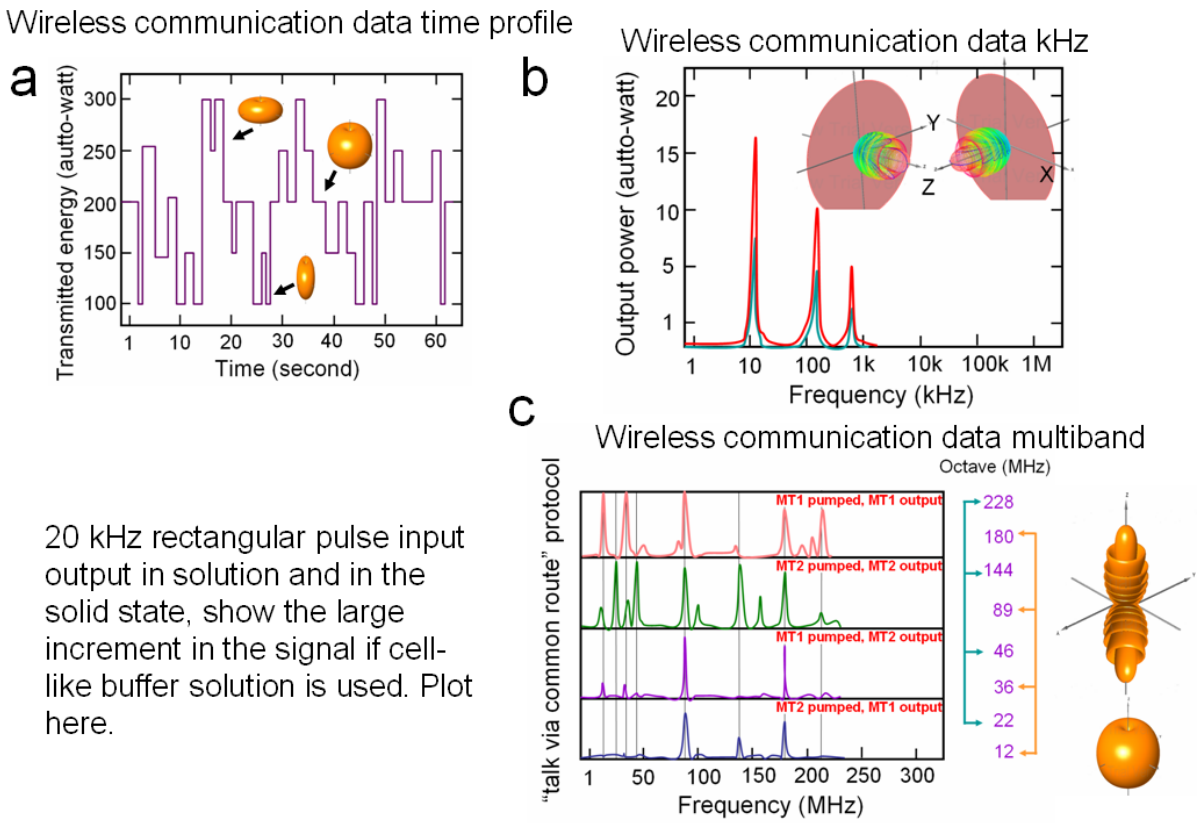
a. AFM image of the Au(111) chip on SiO2 substrate, scale bar 10 μm. Testing circuits for wireless communication between two microtubules, MT1 and MT2 are two microtubules, their perpendicular orientation is shown drawing two lines on the microtubule. b. AFM image of four-probe single microtubule device, scale bar is 400nm. c. The resonance and ac conductivity measuring circuit is shown FG~function generator, inductor L & capacitor C are to block ac and dc signals respectively, RM is dc power transmission & resistance measurement set up.

Figure 3



a. Using the circuit of Figure 1b, dc biased is increased across the microtubule to demonstrate that current output remains constant. b. Resistance distribution on the microtubule surface probed with a fixed 1V bias, for 1.6μm long microtubule. Radiation (10MΩ, red) and transmission domains (300MΩ, green) are marked. AFM image of a microtubule device is shown in the right. L is the distance between AFM tip and the electrode. Figure 2a shows that between ±14V and ±200V dc bias, the output current remains constant at ~±30pA. The current decreases at <14V. Thus, microtubule has fixed allowed channels for the transport of carriers, considering one electron per tubulin, we estimate the channel number as ~108 (30pA/0.1 autto-amp~3×108). c. Schematic of antenna and receiver model used to simulate the electric field distribution. d. A single microtubule is pumped with an ac signal of particular frequency, during pumping dc resistance is measured from both directions, the difference in resistance is plotted for three single microtubule devices 600nm (red), 1μm (green), and 1.6μm (blue) long. Simulated helix antenna feature for a 100 tubulin ring microtubule is shown inset. e. The ac voltage drop across 1μm long microtubule device, temperature was varied from 5K to 320K, ac frequency varied from 10kHz to 20MHz (measurement is done in a shielded chamber, high vacuum 10-6 Torr, sharp fall is at 8.80MHz).

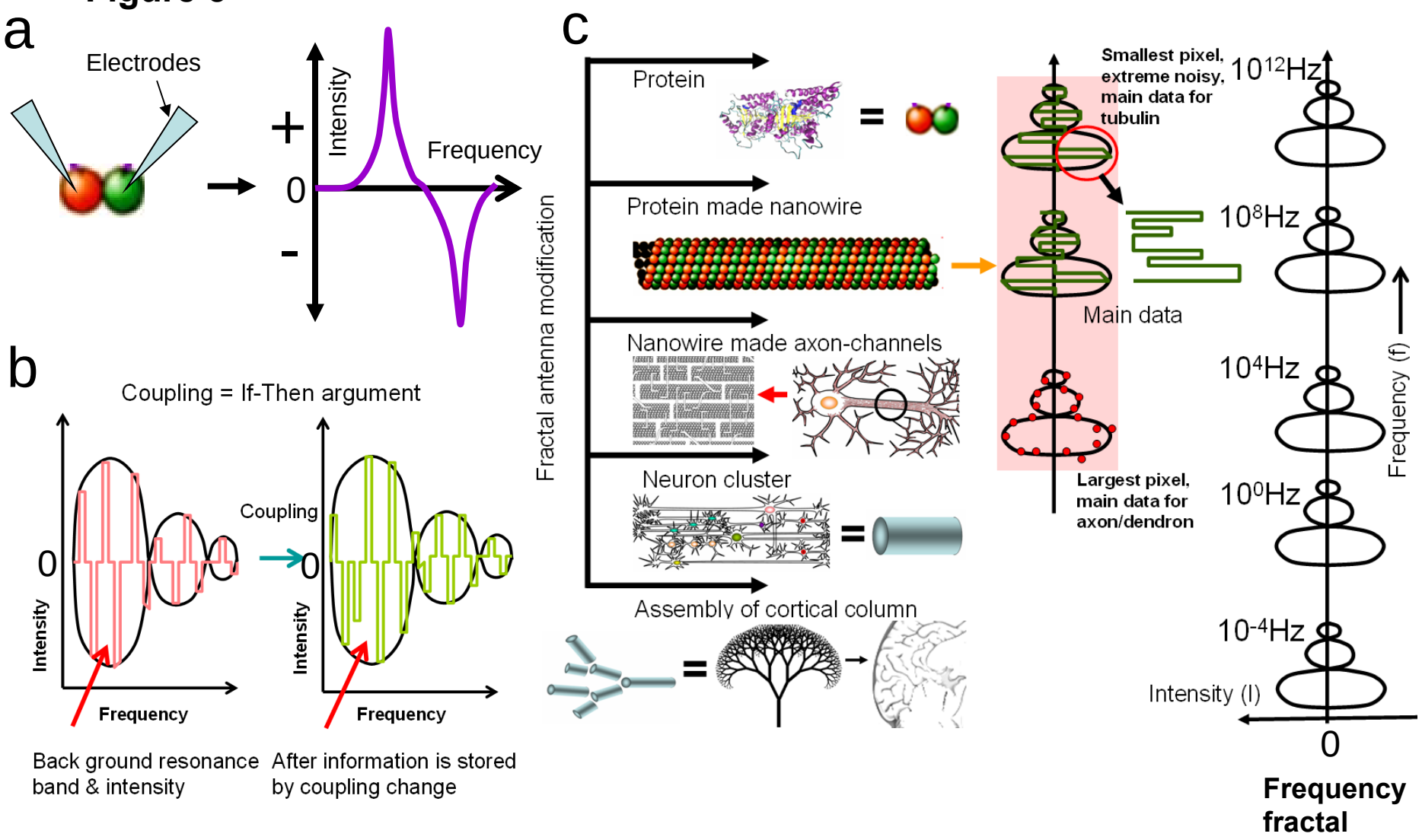
Figure 4



20 kHz rectangular pulse input output in solution and in the solid state, show the large increment in the signal if cell-like buffer solution is used. Plot here.

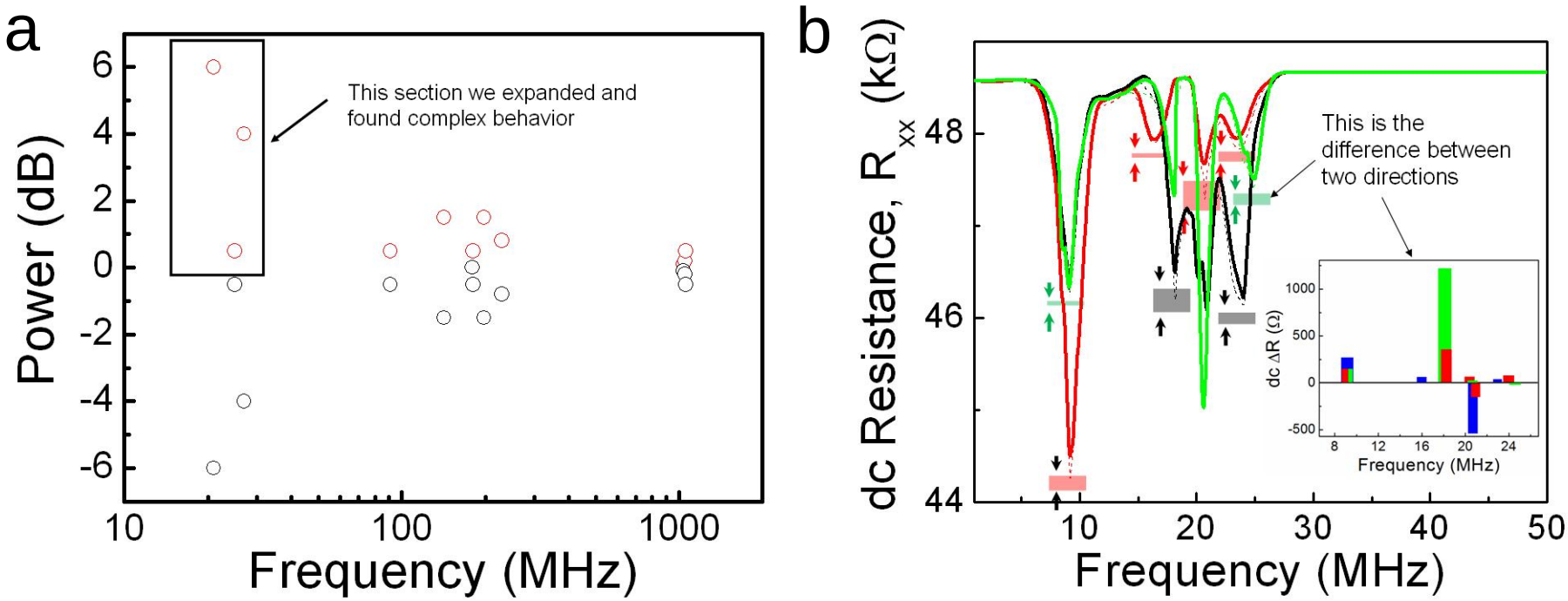
a. Total transmitted energy variation with time, across a single microtubule for 200 autto-watts input, simulated electric field considering single microtubule as dipolar antenna. Electric field variation is shown for particular energy states. b. Wireless transmitted energy for two perpendicularly coupled microtubule devices. The blue plot is for two-isolated microtubule, red plot is for two microtubule bundles located ~20μm apart. Simulated electromagnetic field distributions, for the measuring devices are shown in the inset, considering each microtubule as Helix-antenna. An electrode barrier MN as shown in Figure a, blocks high frequency signal (>800MHz), and we kept a capacitor C to block low frequency signal (<500kHz) yet we see 20 kHz pulsed transmission in a far-distant microtubule. d. Transmission frequencies for four cases, from top, two plots are input/output measurements for single microtubules separately and bottom two plots are cross measurements (input in one, output in another). In its right, statistically favored octave bands of communication and observed coupling between communication frequencies is shown with arrows. Extreme right, generic model of MHz antenna considering both ends of microtubule (top), single microtubule as IR antenna (bottom). An electrode barrier MN as shown in Figure 2a, blocks high frequency signal (>800MHz), and we kept a capacitor C to block low frequency signal (<500kHz) yet we see 20 kHz pulsed transmission in a far-distant microtubule. In Figure 4d, we plot peaks for isolated microtubule M1, M2, and allowed communication channels between the two, thus, the protocol microtubule follows spontaneously, is to "talk via common route".

Figure 5



a. Tubulin protein resonance measurement, intensity of electromagnetic resonance, positive and negative direction, as a function of frequency. b. Main resonance frequency band for a particular oscillator, say, tubulin or microtubule. Background band is the natural band, after conformational/structural change, the band reformats and this information is stored. c. The construction of frequency fractal, complete bands of microtubule is shown.

Figure 6



These two figures are resonance property measurement of a single microtubule device in two different ways.
The first one is measured using two probe cavity resonator device that directly measures the transmission signal.
The bottom one is a four probe manual measurement of resonance peaks using very simple function generator, oscilloscopes, conductivity measurement set up wherein several filters were designed according to need.
The interesting fact about the plots is that in the first we see two side, positive and negative direction values, so it looks like a fractal. However, in the right plot, both positive and the negative plots are in the same direction for three different microtubule lengths. The differences are noted with a gap, the minor differences exist between two opposite direction transmissions.
If we look at the first plot, you can see that the frequency fractal looks like the schematic. Both the plots are same measurement measured and plotted differently. The plot right depicts the symmetry breaking that is actually the changes for information processing.